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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Response to Arguments

Applicant's arguments filed 04/02/08 have been fully considered but they are not persuasive.

112, second paragraph rejection:

Applicant argues that contrast to the Examiner's assertion, the language at issue is submitted to be clear. One of skill in the art would readily understand the above-quoted language to indicate that the patch can deliver amounts of the active ingredient, granisetron, capable of doing that which granisetron is known to do, e.g., prevent nausea and vomiting in a subject undergoing chemotherapy, within 2 hours of being administered to the patient; i.e., invention patches can be administered to a patient, and within 2 hours, chemotherapy can start. Consistent with this discussion, the Examiner's attention is directed to paragraph [0035] of Applicants' specification, which indicates that "the patches of the present invention can already begin to show efficacy by about 2 hours..."

However, while the examiner agrees to applicant's remarks, it appears that the above remarks are contradicting to the limitation in claim 9 because claim 9 specifically recites a patch adapted to "provide a pharmacologically effective amount of granisetron *after* about 2 hours". Thus, the limitation "after about 2 hours" includes 3 hours, 4 hours, 24 hours, and so on. However, the present specification discloses *levels associated with the patches of the present invention can already begin to show efficacy by about 2 hours, so that patches of the invention can be useful in the treatment of acute emesis*. Accordingly, the claim is indefinite because it is not entirely clear when

the "pharmacologically effective amount of granisetron" be provided. When exactly is after about 2 hours? Accordingly, the 112, second paragraph rejection of claim 9 is maintained.

102(b) rejection by Effing:

Applicant argues that in contrast to the present claims, which are directed specifically to adhesive patches containing granisetron, Effing is directed to adhesive patches containing either tropisetron or granisetron--suggesting that these two compounds are substantially similar both structurally and functionally (see, for example, page 1, line 23-page 2, line 2 of Effing, which suggests the interchangeability of these compounds). Indeed, as discussed at the personal interview, virtually every reference to active drug in the Effing specification is made in the alternative:

-in the Title ("TROPISETRON OR GRANISETRON");

-in the abstract, line 5 ("selected from the group consisting of tropisetron and granisetron");

-in the abstract, line 7 ("tropisetron or granisetron");

-page 1, line 6 of the specification ("tropisetron or granisetron");

-page 1, lines 23-24 of the specification ("Tropisetron... and granisetron");

-page 2, line 20 of the specification ("tropisetron and granisetron");

-page 2, line 28 of the specification ("tropisetron and granisetron"); and

-page 7, line 24 ("tropisetron or granisetron").

The only exceptions throughout the Effing specification where tropisetron and granisetron are not mentioned in the same clause are found:

-in the background (at page 2, line 10) where "ondansetron and granisetron" are suggested to be interchangeable; and

-in the Examples, which deal only with tropisetron; however, based on the consistent indication throughout the Effing specification that tropisetron and granisetron are substantially interchangeable, there is no reason (absent improper reliance on Applicants' disclosure) why one of skill in the art would expect granisetron to perform any differently than tropisetron.

Moreover, not only does Effing teach the interchangeability of tropisetron and granisetron, the reference also teaches the undesirability of using hydroxyl-containing monomers (such as HEA) in the preparation of an adhesive patch containing tropisetron or granisetron. Indeed, the reference clearly teaches away from the use of any hydroxyl-containing monomer, such as HEA, in the preparation of an adhesive patch containing tropisetron or granisetron, as evidenced by the numerous admonitions throughout the Effing specification that the B monomer should be free of nucleophilic groups (including hydroxyl):

-page 3, line 24 of the specification ("Preferably, the B monomer is free of nucleophilic groups");

-page 3, line 30 - page 4, line 1 ("Preferably, the B monomer is free of nucleophilic groups");

-page 4, lines 8-9 ("Such monomers are preferably free of groups containing nucleophilic groups as described above");

-claim 2, lines 1-2 ("said B monomers are free of nucleophilic groups");

-claim 3 lists numerous possible B monomers, but hydroxyl-containing monomers are conspicuously absent from the list of possibilities;

-claim 12, lines 1-2 ("said B monomers are free of nucleophilic groups"); and

-claim 13 lists numerous possible B monomers, but hydroxyl-containing monomers are conspicuously absent from the list of possibilities.

Thus, repeatedly throughout their disclosure, Effing asserts that "preferably, the B monomer is free of nucleophilic groups." Indeed, the numerous admonitions throughout the Effing specification that the B monomer should be free of nucleophilic groups are fully consistent with the results of EXAMPLE 7 (at page 13 of Effing), which indicates that an adhesive prepared with 2-hydroxyethylacrylate (HEA) as monomer B suffered from a decrease in drug content of more than 10% within four weeks of storage. This stands in stark contrast to the remaining examples which evaluate the stability of the active drug in the transdermal patch. See, for example, EXAMPLE 1 and EXAMPLE 2 (both at page 11 of Effing), which indicate that full stability is retained at both 25°C and 40°C for at least four weeks with the adhesive formulations employed therein (which include no hydroxyl-containing monomers).

However, applicant's arguments over Effing are not found to be persuasive for the following reasons:

i) Effing does teach the use of the claimed compound for the same purpose, namely, granisetron in an adhesive patch for the transdermal administration;

ii) Effing does teach the use of the claimed non-acidic hydroxyl moieties such as 2-hydroxyethylacrylate (see page 3, lines 13-14);

iii) applicant compares the stability of the claimed invention and that of Effing, however, the present claims do not require any storage conditions, let alone the specific storage condition taught in example 7 of Effing;

iv) although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993);

v) example 7 discloses stability study for tropisetron, not granisetron;

vi) dependent claim 7 of the present application recites the adhesive patch further comprises *a major amount of a primary acrylate monomer*, leaving the amount for the non-acidic hydroxyl moieties, indeed, minor; and

vii) example 2 of the present specification does not disclose the structure of the patch, *e.g.*, what monomer, what non-acidic hydroxyl moieties, and in what amounts were used for the stability study. In contrast, Effing at page 3, line 14, teaches B monomer includes HEA. Applicant directs the Examiner's attention to example 7 in Effing for the teaching of the storage stability, it is noted that example 7 is directed to a different compound, e.g., tropisetron. Further, a reference may be relied upon for all

that it would have reasonably suggested to one having ordinary skill the art, *including nonpreferred embodiments*. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). Moreover, it is noted that the claimed adhesive patch is not entirely composed of HEA, per se. This is evident by claims 7 and 8 of the present invention, which recite a patch that "containing a *major* amount of a primary acrylate monomer" selected from either 2-ethylhexyl acrylate or butyl acrylate. These polymers do not contain non-acidic hydroxyl moieties.

For the above reasons, the 102(b) rejection over Effing is maintained.

Applicant argues that reliance on Sanger is unable to cure the deficiencies of Effing, since Sanger adds nothing to the consideration of what a transdermal patch for the delivery of granisetron should look like.

In response to applicant's argument, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Sanger is relied upon solely for the teaching that 5-HT_3 receptor antagonist such as granisetron is known for the treatment of visceral pain and migraine (abstract).

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 8:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/S. Tran/
Primary Examiner, Art Unit 1618